CLAIM AMENDMENT

1. (Previously presented) A method of obtaining a bacterium comprising a nucleic acid sequence encoding a binding protein that binds a target ligand comprising the steps of:

(a) providing a Gram negative bacterium comprising a nucleic acid sequence encoding a candidate binding protein, wherein said binding protein is expressed in soluble form in the periplasm of said bacterium;

(b) contacting said bacterium with a labeled ligand that diffuses into said periplasm; and

(c) selecting said bacterium based on the presence of said labeled ligand within the periplasm, wherein said ligand and said candidate binding protein are bound in said bacterium.

2. (Currently amended) The method of claim 1, further ~~defined as a method of obtaining a nucleic acid sequence encoding a binding protein, the method further~~ comprising the step of:

(d) cloning said nucleic acid sequence encoding said candidate binding protein.

3. (Canceled)

4. (Previously presented) The method of claim 1, wherein said nucleic acid sequence encoding a candidate binding protein is further defined as operably linked to a leader sequence that directs expression of said candidate binding protein in said periplasm.

5. (Original) The method of claim 1, wherein said Gram negative bacterium is an *E. coli* bacterium.

6. (Original) The method of claim 1, further defined as comprising providing a population of Gram negative bacteria.

7. (Previously presented) The method of claim 6, wherein said population of bacteria is further defined as collectively expressing a plurality of candidate binding proteins.

8. (Previously presented) The method of claim 7, wherein said population of bacteria is obtained by a method comprising the steps of:

(a) preparing a plurality of DNA inserts which collectively encode a plurality of different potential binding proteins, and

(b) transforming a population of Gram negative bacteria with said DNA inserts.

9. (Original) The method of claim 6, wherein said population of Gram negative bacteria is contacted with said labeled ligand.

10. (Original) The method of claim 1, wherein said candidate binding protein is further defined as an antibody or fragment thereof.

11. (Original) The method of claim 1, wherein said candidate binding protein is further defined as a binding protein other than an antibody.

12. (Original) The method of claim 1, wherein said candidate binding protein is further defined as an enzyme.

13. (Previously presented) The method of claim 1, wherein said candidate binding protein is further defined as not diffusing out of said periplasm in intact bacteria.

14. (Original) The method of claim 1, wherein said labeled ligand comprises a peptide.

15. (Original) The method of claim 1, wherein said labeled ligand comprises a polypeptide.

16. (Original) The method of claim 1, wherein said labeled ligand comprises an enzyme.

17. (Original) The method of claim 1 where said labeled ligand comprises a nucleic acid.

18. (Original) The method of claim 1, wherein said labeled ligand is further defined as comprising a molecular weight of less than about 20,000 Da.

19. (Original) The method of claim 1, wherein said labeled ligand is further defined as comprising a molecular weight of less than about 5,000 Da.

20. (Original) The method of claim 1, wherein said labeled ligand is further defined as comprising a molecular weight of greater than 600 Da and less than about 30,000 Da.

21. (Original) The method of claim 1, wherein said labeled ligand is further defined as fluorescently labeled.

22. (Previously presented) The methods of claim 1, wherein said nucleic acid encoding a candidate binding protein is further defined as being amplified following said selection.

23. (Previously presented) The method of claim 1, further comprising treating said bacterium to facilitate diffusion of the labeled ligand into said periplasm.

24. (Original) The method of claim 23, comprising treating the bacterium with hyperosmotic conditions.

25. (Original) The method of claim 23, comprising treating the bacterium with physical stress.

26. (Original) The method of claim 24, comprising treating the bacterium with a phage.

27. (Original) The method of claim 1, wherein said bacterium is grown at a sub-physiological temperature.

28. (Original) The method of claim 27, wherein said sub-physiological temperature is about 25°C

29. (Original) The method of claim 1, further comprising removing labeled ligand not bound to said candidate binding protein.

30. (Previously presented) The method of claim 1, wherein said selecting comprises fluorescent activated cell sorting.

31. (Original) The method of claim 1, wherein said selecting comprises magnetic separation.

32. (Original) The method of claim 1, wherein said ligand and said candidate binding protein are reversibly bound in said periplasm.

33.-74. (Canceled)